II. Obviousness Rejection

Applicants continue to traverse the obviousness rejection of Claims 1 to 4, 10 to 14, 18, 19 and 23 over Bao and refer the Examiner to the arguments made in the Applicant's reply dated March 23, 2009. Additional arguments in support of patentability are set forth below.

The Examiner argues that it would have been obvious for one skilled in the art to select Example 18 from Bao and modify the compound by replacing the methoxy group with chlorine and substituting pyridyl for phenyl. At page 6, the Examiner states that the "person of ordinary skill in the art at the time the invention was made would have been motivated to make the bioisosteric modification to synthesize ***similar compounds that retain biological activity***, but have improved physiochemical properties and better pharmacokinetic behavior." (emphasis added) At page 7, the Examiner further asserts that since "the compounds taught by Bao are "potassium channel inhibitors" the skilled artisan would have predicted that the well known bioisosteric modifications taught by *Williams et al* and *Patani et al* – when applied to the potassium channel inhibitors taught by *Bao et al* – ***would provide compounds having similar activity*** as potassium channel inhibitors, but with distinct pharmacokinetic profiles." (emphasis added)

Applicant refer the Examiner to Lindsley et al., *ChemMedChem* **2006**, 1, 807-811 ("Lindsley"), which has been submitted in an Information Disclosure Statement herewith. Lindsley at page 808 states the following:

> As shown in Table 1, a variety of functionalized benzamides are tolerated, and not only dramatically improve GlyT1 potency while maintaining high selectivity, but also abolish the ancillary potassium channel activity. Clearly, the 2-OMe benzamide moiety was the key to the undesired ancillary potassium channel activity, as unsubstituted phenyl **8a**, 2-halogen substituted analogues **8c** and **8d**, and 3-OMe and 4-OMe (data not shown), possess no potassium channel activity.

Applicants submit this evidence further supports the Applicants position that Claims 1 to 4, 10 to 14, 18, 19 and 23 are non-obvious over Bao. First, the evidence demonstrates the high unpredictability of the art, with small changes in structure having a large impact on activity. *See* M.P.E.P. 2144.08(e): "If the technology is unpredictable, it is less likely that structurally similar species will render a claimed species obvious because it may not be reasonable to infer that they would share similar properties." Second, the evidence undercuts the Examiner's argument that it would have been obvious to modify the compounds of Bao by substituting chlorine for the 2-methoxy group with a reasonable expectation of retaining potassium channel activity. **All** the examples disclosed in Bao contain the 2-methoxy

group on the benzamide portion of the molecules. In Bao, there is no disclosure of examples having other than the 2-methoxybenzamide structure being actually made and tested for potassium channel activity. Modification of the 2-methoxy group on the benzamide portion results in loss of potassium channel activity. Since all the actual examples in Bao are 2-methoxybenzamides, one skilled in the art would in no way be motivated to modify the 2-methoxy portion of the molecules over the many other modifications that are possible. Applicants assert the Examiner is relying on impermissible hindsight in rejecting the present claims as obvious. Withdrawal of the obviousness rejection of Claims 1 to 4, 10 to 14, 18, 19 and 23 over Bao is respectfully requested.

III. Double Patenting Rejection

Applicants request the provisional obviousness-type double patenting rejection be held in abeyance until the claims are otherwise found allowable.

IV. Rejoinder

Withdrawn Claims 9 and 20 are directed to Group I subject matter and should be rejoined. Rejoinder of the method claims 24 to 27 pursuant to M.P.E.P. § 821.04 is also respectfully requested.

VI. Conclusion

An early and favorable examination is earnestly solicited.

Respectfully submitted,

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